III.
2b Liver

Already in earlier experiments (DONTENWILL and EDER (1959), DONTENWILL and MOHR (1961), we frequently observed single or multiple cysts of the bile-duct, to some extent arranged in conglomerates, in the liver of goldhamsters (ill. 24). As formerly, we distinguished between liver cysts and the so-called cyst-liver in which the entire liver is penetrated by numerous cysts and the extremely enlarged organ shows only remains of parenchyma between the densely settled cysts (ill. 25). The evaluation of the test results shows that the frequency of cysts is larger in the female animals, but that a significant difference can not be proven because of the strong dispersion. A correlation to sex of the cyst-liver is not recognizable. ($X^2 = 3.26$ with 1 FG; ($P > 5\ \%$). An increase in cysts, as we and others had formerly observed in the carcinogen treatment of the liver (LAUBER and DANNENBERG (1956), DONTENWILL and MOHR (1961 a plus b), DONTENWILL (1961), BANHASCH and REISS (1971), RIVIÈRE and OBERMAN (1967), is not provable in the smoke-exposed animals. - Cysts in other organs, we were able to trace only very sporadically, they occured in the suprarenal gland, the kidney and the pancreas. -

According to the observations, respectively experiences made earlier, an increase in liver cysts, respectively the cyst-liver in the treated groups could have been understood as an expression of the proliferation-triggering effect of smoke-substances in the area of the liver, this was not recognizable (chart 46).

As in a second essential change, we were interested in the appearance of parasitic granulomatoses, respectively other inflammable liver diseases and bile-duct inflammations respectively bile-duct proliferation. These changes could yield information on toxic damages of the liver parenchyma, respectively on the triggering of proliferative changes which, with the effect of weak carcinogens, often precede the development of cirrhosis and carcinoma formation. Chart 47 shows the frequency distribution of these diseases. Neither ~~Neither~~ the frequency of hepatitis (which also contains granulomatous forms)

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Source: https://www.industrydocuments.ucsf.edu/docs/ylkk0000

nor that of the liver abscesses or that of cholangitis shows a correlation to the treatment. Liver necroses which did not occur at all frequently, were very rarely observed in the smoke-exposed animals.

In the frequency of the hemosiderin deposits of the liver (particularly in Kupffer's Starcells), it is conspicuous that the animal groups I2 - I8A, included into the test later, respectively delivered later, are almost free of hemosiderin deposits. There are no significant differences between the smoke-exposed groups 4, 5 and 6 and contro group 3 ($X^2 \leq 2.02$ with 3 FG; (P> 5 %)). There is also no significant difference in the hemosiderin frequency between males and females ($X^2 \leq 0.30$; I FG; (P> 5 %)). Bile-duct proliferations which are often an expression of the first reaction of the liver tissue did not occur more frequently in the treated animals. A liver cirrhosis was not observed in any animal.

Liver tumors occured only with minimal frequency in our stock, chart 48.

It is a case of typically metastasizing bile-duct carcinomas (ill. 26), malignant hepatomas (ill. 27), of hemangioendotheliomas and of benign tumors like hemangiomas and papillary bile-duct adenomas. The total number of the occuring benign tumors does not allow for an indication of a change caused by the treatment. Solely in malignant liver tumors, a frequency increase ensues in the male animals treated with DMBA.

The frequency of liver cirrhoses, respectively primary liver tumors or bile-duct tumor was obviously much higher in other hamster colonies. CHESTERMAN and POMERANCE described 1965 a frequency increase of liver cirrhosis up to 20 % whereby 6 % of the animals with cirrhoses of the liver had liver tumors. FORTNER (I957 a, I958) among others, reported on spontaneous tumors among 620 hamsters

= 20 liver and bile-duct carcinomas

FORTNER (I96I) among I8I hamsters

= 8 liver carcinomas

KIRMAN (I962) among 7200 hamsters

= 94 hepatomas
7 malignant hepatomas
4 cholangiomas
2 malignant cholangiomas

SICHUK, FORTNER, DER, RUSSFIELD (I966) among 79 hamsters

= I bile-duct carcinoma

TOMATIS, DELIA PORTA, SHUBIK (I96[illegible]) among 63 hamsters

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Source: https://www.industrydocuments.ucsf.edu/docs/[illegible]

= I angioma of the liver

LEE, TOTH and SHUBIK (I963) among 54 hamsters

= I cholangioma

TOTH (I967) among 200 hamsters

= 2 cholangiomas
2 cholangiocarcinomas

HORN and SIEMERT (I968) among I630 hamsters

= I carcinoma

KIRKMAN (I950) among 5I hamsters

= I hepatoma

DELLA PORTA, SHUBIK and SCORTECCI (I959) among I5I hamsters

= I cholangioma

FORTNER and GALE (I958)

= 2 bile-duct adenocarcinomas.

After DMBA treatment, I cholangiocarcinoma among 24 hamsters was proven in the experiments of RAPPAPORT, PIETRA and SHUBIK (I96I). SHUBIK and Assoc. (I962) found after DMBA treatment of the skin (I02 animals), I cholangiocarcinoma and I cholangioma, after endotracheal application I cholangioma. They had also described tumors of the trachea, the larynx, the bronchi, the skin, the stomach, the intestines and the mamma as well as the ovaries after DMBA treatment. TOTH (I969) found among 60 hamsters, treated with DMBA over a longer period of time, I hemangiosarcoma of the liver besides 2 stomach sarcomas, 4 mamma carcinomas, 5 papillomas of the tubes and I hemangiosarcoma of the spleen.

We discussed the frequency of liver amyloidosis in the chapter "General Amyloidosis".

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Source: https://www.industrydocuments.ucsf.edu/docs/ylkk0000

III.

2c Gastro-intestinal Tract

Because of the postulated association between the smoking of cigarettes and the formation of the peptic stomach ulcer (see also SCHIEVELBEIN, I968), we were particularly interested in the frequency of stomach ulcers in the different test groups of our test stock.

FORTNER reported I957 already on the spontaneous occuring of stomach ulcers in goldhamsters.

It is understandable that we were also interested in the question of the spontaneous frequency of benign and malignant stomach tumors in view of the varied treatment of the test animals.

There had been several reports on spontaneous stomach tumors in goldhamsters. FORTNER (I957, I958) described among 620 hamsters a total of I24 tumors (carcinomas, sarcomas polypi) in the gastro-intestinal tract, and I96I among I8I hamsters I2 omasum papillomas and 3 carcinomas (stomach). TOMATIS and Assoc. (I96I) saw 3 papillomas among I03 hamsters, DUNHAM and HERROLD (I962) I carcinoma among 360 hamsters, LEE and Assoc. (I963) 2 omasum papillomas among 54 hamsters, and TOTH (I967) 8 omasum papillomas among 200 hamsters, whereas KIRKMAN (I962) found among 7200 hamsters no stomach carcinoma but one duodenal polypus. Polypi of the glands of the stomach were described rarely (FORTNER I96I and DUNHAM and HERROLD I962). Polypi in the intestines were described by FORTNER (I96I), DELLA PORTA (I962) and SICHUK and Assoc. (I966). FORTNER and GALE (I958)found one adenocarcinoma in the intestines.

Stomach tumors were frequently observed after treatment with carcinogens. After oral application of DMBA, CHU and MALMGREN (I965) saw carcinomas of the omasum. After intravenous dispensal of DMBA, TOTH (I969) observed 47 papillomas of the omasum and I3 omasum carcinomas as well as sporadic polypi and carcinomas of the intestines among 60 hamsters. DELLA PORTA and Assoc, (I958) found after multiple intratracheal application of DMBA in one of 7 surviving hamsters an esophagus carcinoma.

We were able to prove the following changes in the individual sections of the gastrointestinal tract:

I. In the esophagus we found papillary growths of the pavement epithelium (ill. 28) only in the animals pretreated with DMBA, chart 50. Only once, group 8, we observed in a not-treated animal a beginning pavement epithelium carcinoma (ill. 29) of the mucous membrane of the esophagus. A correlation between treatment and tumor formation

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Source: https://www.industrydocuments.ucsf.edu/docs/ylkk0000

in the esophagus could not be proven.

2. In the stomach we found with differing frequency fresh and older ulcerations of the mucous membrane which were already macroscopically recognizable in some instances. Chart 50 shows the frequency of the stomach ulcera in the individual test groups.

A significant increase of the stomach ulcera in the smoke-exposed animals, particularly in dependence from the dose, was not provable in comparison to the not smoke-exposed groups 3 and 8 ($X^2 = 8.49$ with 4 FG ($P > 5\ \%$)).

The frequency of gastritis too, did not differ between smoke-exposed and not smoke-exposed animals (chart 5I). Here, we only termed diffuse, strongly inflammable infiltrations of the mucous membrane of the stomach as gastritis.

In test and control animals, we observed typical stomach papillomas (ill. 30) of morbidly growing multi-layered pavement epithelium of the mucous membrane of the omasum. These stomach papillomas were unequivocally more frequently provable in the animals pretreated with DMBA. (Difference between the groups I, 2 and 3 : $X^2 = 203.4$ with 2 FG ($P < I\ \%$)). Chart 5 (next number illegible, Tr.) shows the frequency distribution of the papillomas of the stomach. Smoke-exposed animals showed no increase in stomach papillomas (difference between the groups 3, 4, 5 and 6 : $X^2 = I.36$ with 3 FG ($P > 5\ \%$)). Besides benign papillomas, we also observed infiltratively growing, to some extent, keratinized pavement epithelium carcinomas of the omasum (ill. 3I), (chart 50). Here too a greater frequency was evident solely in the male animals pretreated with DMBA (difference between the groups K, I, 2 and 3 : $X^2 = I0.4$ with 3 FG (P approximately I $\%$). Carcinomas of the stomach glands were not provable. An increase of stomach tumors in the smoke-exposed animals, in dependence from the dose, was not provable in comparison to the control animals.

3. Intestinal Diseases: Among the intestinal diseases, unspecific inflammabel diseases

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Source: https://www.industrydocuments.ucsf.edu/docs/ylkk0000

and invaginations must be separated from parasitic diseases and the intestinal disease which is termed "wet tail".

Upon dissection, a moderate to intermediate infestation with syphacia obvelata (oxyuridea) was found in several animals. The sexually mature worms were discovered in the coecum and colon.

A larger number of hamsters fell ill, approximately 15 to 20 days after their arrival with an extreme enteritis which presented itself as an ileitis terminalis, respectively a typhilitis and is known in the American literature as "wet tail" of the hamsters. Clinic and pathology of the disease are in accord with corresponding descriptions by SHEFFIELD and BEVERIDGE (1962), HANDLER (1965) as well as JONAS and Assoc. (1965). Frequency, see chart.

The disease starts with a diarrhoea which moistens the tail region of the animals. Within a few days the animals become emaciated and die within from 48 hours to one week after begin of the symptoms. Inflammations of the ileum and coecum are pathologically-anatomically prominent. They are combined with an extreme thickening of the intestinal walls, diptheroid coatings and ulcerations which perforate occassionally. Few animals survive the acute illness and die subsequently of complications like adhesive peritonitis, abscesses in the mesentery, scar-strictures as a result of the ulceration.

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Histologically recognizable is first of all, in the area of the mucous membranes of the ileum and coecum, an intermediate to extreme inflammable infiltration of the mucosa with desquamation of the epithelium and formation of diptheroid coatings. This is followed by a regenerative, strongly hyperplastic new formation of epithelium with distinct cell polymorphy and numerous mitoses (ill. 32 a - c). This pattern caused JONAS and Assoc. (1965) to speak of an enzootic adenocarcinoma. Numerous necroses of the mucosa were found besides the hyperplastic changes, they can focally extend through the muscularis as far as the serosa.

Source: https://www.industrydocuments.ucsf.edu/docs/ykkf0000

No specific viruses could be indentified through the bacteriological examination. Neither prohylactically, as SHEFFIELD and BEVERIDGE (1962) suggested, nor therapeutically was it possible to exert an influence on the course of the disease with neomycin-sulfate. In the initial phase of the test, a total of 489 animals per group died of "wet tail".

A relatively frequent cause of death were intestinal invaginations. Occassionally, they were combined with inflammable changes, but in most instances, they occured in already emaciated animals of advanced age.

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Source: https://www.industrydocuments.ucsf.edu/docs/jlkk0000

III.

2d Cardiovascular System

Numerous researchers have been concerned with the question of the effect of smoke-substances on the heart and the circulatory system.

While, up to a few years ago, nicotine was predominantly held responsible for the supposable effect of smoke-substances on man (see AUERBACH and Assoc. I965), CO is being included into the discussion as an essential factor, to an increasing extent, through the experiments of ASTRUP and Assoc. (I970) as well as other researchers, eventhough the findings postulated for the rabbit did not occur in other animal breeds (monkeys, dogs, rats and mice) with an, to some extent, extreme CO-concentration (THEODORE and Assoc. I97I).

Through chronic application of nicotine, particularly in combination with an atherogenic diet, an increase of the tendency to arteriosclerosis was observed in the rabbit. The test results after experiments with pure nicotine application are very varied. SCHIEVELBEIN and EBERHARDT (I972) drew the conclusion, "that nicotine alone, even in a high dose, cannot produce any degenerative vascular changes, even in a species very susceptible to developing an arteriosclerosis, but that it shows an effect as an additional factor" (lit. in: The Health Consequences of Smoking I97I/I972). After intoxication with CO, an accumulation of arterioscleroses was observed in the rabbit (ASTRUP and Assoc. I967). Literature in : The Health Consequences of Smoking I97I, I972, SCHIEVELBEIN and Assoc. (I970). After chronic smoke-treatment of dogs, AUERBACH and Assoc. (I97I) saw an increase of sclerotic vascular changes particularly on the heart. Upon critical evaluation of the entire test results with nicotine, CO and total smoke treatment, it becomes evident that the effect obviously fluctuates extraordinarily from one animal breed to another and is largely dependent on the food supplied to the animals.

Earlier observations on inflammable vascular diseases after nicotine influence (lit. see LARSON and Assoc. I96I) are difficult to evaluate because a comparison with contr[illegible] groups of the same age is often missing in the tests. This holds true, to some extent, for examinations of not inflammable vascular diseases, particularly in larger control groups of dogs (CHEVALIER and KERSTEN I970) where vascular wall changes (hyalin-fibro[illegible] swelling) were observed in statistically significant frequency with increasing age.

A number of experiments was concerned with the sebacic acid metabolism of the animals after nicotine treatment as well as total smoke treatment. While predominantly increa[illegible] of the free sebacic acids, but to some extent also an increase in the cholesterol level were observed in man, the experimental tests show very varied findings for the effect of nicotine and total smoke (lit. in: The Health Consequences of Smoking, I97I, I972 as well as KERSHBAUM I967).

Already earlier, we reported (REICKZEH and DONTENWILL I970) on an increase of the erythrocytes after chronic smoke-treatment of the goldhamster. We attributed this erythrocyte increase to the chronic co-intoxication which takes place in our smoke-treatment method through the interval-free smoke inhalation lasting over a longer period of ti[illegible]. Our experiments DONTENWILL and Assoc. (I967) demonstrated, that with the high-dose smoke-treatment, up to 20 % CO-Hb is produced daily, which means, quantities which are not observed in man even in extreme instances. The persistent relative oxygen deficit is obviously compensated in the hamster through an increase of the erythrocytes.

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That proves that a maximal CO-inhalation took place in the technique which we chose, and that we can also count on a high inhalation of other smoke-substances.

Since, as we were able to observe already earlier, a severe vascular amyloidosis of the kidneys with, to some extent, considerable shrinking appears in the hamster with increasing age, which must necessarily lead to a resistance rush, several components like nicotine, and CO-effect as well as hypertonia concur in the test arrangement. This was the reason why it seemed informative to examine the effect of the smoke-treatment on the sebacic acid metabolism in order to be able to better evaluate the postulated findings (see chapter 3).

Vascular wall changes in the sense of an arteriosclerosis were observed in the hamster after a "cholestrol diet" by ALTSCHUL (1946, 1950) and DEUEL (1947). Other authors like GOLDMAN (1950) were not able to confirm these experiments. Whether the observations of ALTSCHUL (1946) are cases of an arteriosclerosis, is doubtful, since a part of the vascular changes corresponds fully with the vascular amyloidoses observed by us. HANDFORTH (1962) described necrotizing arteritis and heart infarcts in the hamster after treatment with isoproterenol. FORTNER (1957) observed perivascular inflammations, hyaline vascular necroses of the arterioles, vascular thromboses as well as inflammable diseases of the myocardium and endocardium as spontaneous diseases in the hamster.

In our tests, we predominantly examined four vascular sections: vessels of the heart and the lung, changes on the aorta ascendens as well as stomach aorta and the pelvic arteries.

The vascular changes observed in all four sections were essentially cases of <u>inflammable vascular diseases</u>. These showed a vastly uniform pattern. They could be summarized under the term of thromarteriitis. All the morphological changes, also observed in man, which were described under these disease designations, like fibrinoid swelling, fibrinoid necrosis, proliferation of the endothelium, inflammable infiltration in the vascular wall and vascular vicinity were provable in the same way as beginning aneurysmatic bulging of the vascular walls. This is easily recognizable by comparisons on hand of the evaluations (charts 53 and 54). Inflammable vascular changes were in the lung more frequently combined with vascular thrombi, see chapter Respiratory Tract. 1002968612

<u>Chief localization of the inflammable vascular diseases were the large coronaries</u> (ill.33)

Source: https://www.industrydocuments.ucsf.edu/docs/xyb0065

and the pelvic vessels (ill. 34). Inflammable changes of the aorta ascendens were observed only very rarely, but they were often severe and, predominantly in the chest section, combined with aneurysms respectively ruptures of the aorta which is demonstrated by illustration 35. The relatively small frequency of inflammable vascular diseases complicates the evaluation of the question, whether the smoke-treatment has led to an increase in vascular diseases. The inflammable diseases of the coronary vessels were in the female animals highly significant , with variances more frequent than in the male animals ($x^2 = 54.9$ with I FG; ($P < I\ \%$)). In female animals which show a shorter survival period - apparently due to frequent inflammable diseases - the number of coronary inflammations is, to some extent, distinctly higher in the smoke-exposed animals as compared to the not-treated animals. This holds true particularly for the groups I4, I5, I6 and I8 in comparison to control group 3. However, the frequency in group 6 is not significantly higher in contrast to group 3 ($x^2 = 2.I5$ with I FG; ($P > 5\ \%$)). The number of coronary inflammations after smoke-treatment is not higher with certainty in the male animals. The frequency rests in almost all the groups approximately at I %. Solely in group I5, 5% of the male animals had coronary inflammations. Inflammations of the large vessels of the pelvic and the upper thigh also occured unequivocally more frequently in female animals ($x^2 = 37.7$; I FG; ($P < I\ \%$)). An unequivocal frequency increase in the smoke-exposed animals as compared to the controls (groups K, 3 and 8) was not provable ($x^2 = I4.73$ with 5 FG; ($P > I\ \%$)).

In contrast to that, we were able to prove calcifications of the vessels of the media only in one animal of group K in the area of the aorta (ill. 36) and the large vessels of the pelvis. In examining the mentioned vascular sections, we saw no clues which would point to unequivocal vascular changes, comparable to arteriosclerosis, as they are described, analogus to man, in the monkey or the pig.

Among the observed diseases of the heart, two groups must be distinguished:

I. inflammable heart diseases,

2. degenerative diseases of the heart muscle.

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Source: https://www.industrydocuments.ucsf.edu/docs/jkk0099

Among the inflammable heart diseases, diseases of the cardiac valves stand in the foreground. We compiled their frequency distribution in the subsequent chart 55. These cardiac valve diseases are cases of endocarditis in all degrees (ill. 37 a, b and c) beginning with a swelling of the cardiac valves and inflammable infiltration to a maximal polypoidi coating of thrombi which, in parts, completely block the flow-out path. Chronic endocardites with fibrosis and calcification were also observed. Chief localization of the endocarditis were, in the same sequence as in man, the mitral valve and the aortic valve and the tricuspid valve. Occasionally, the inflammable valve changes also extended to the mural endocardium, from the aorta valve also to the aorta. In a large number of animals of all the groups, extensive thrombi were found predominantly in the left atrium (Vorkammer) (Ill. 38) which often filled the vena cava inferior (Vorhof) and the auricle (Herzohr) completely. An obvious correlation between these thrombi and the valve thrombi is provable only in one of the cases. There is no correlation to the treatment.

Besides these inflammable valve changes, we observed the already described changes in the sense of the arteriitis and periarteriitis of the coronaries. Thereby we counted fibrinoid swellings among the inflammable vascular ~~changes~~ diseases since they must be considered preliminary stages of these inflammation processes according to general experience.

Inflammable vascular changes of the aorta were rare and occured only in female animals. This fact demonstrates a parallelity to the vascular inflammations of the heart which occured more frequently in female animals. Aneurysms of the aorta were also more frequent in female animals. Parietal thrombi of the aorta occured only in one control animal. Besides the described inflammable vascular changes, vascular processes within the scope of an amyloidosis were prominent, as we described them particularly in the liver, kidney, spleen, suprarenal gland and in the testicles (see page).

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In this context we were interested in the comparison between body weight, heart weight, kidney weight. The comparison between body weight and heart weight (charts 56 - 63) as

Source: https://www.industrydocuments.ucsf.edu/docs/[illegible]

well as kidney weight was intended to give a clue on the presence of a rise in blood-pressure. An increase of the heart weight with hereditary muscle degeneration was described by ONISHI and Assoc. (1970). The mentioned correlations are discussed in the following.

Correlation between Heart Diseases, End-Weight, Survival Period, Heart Weight, Kidney Weight

In the charts 56 - 63 the average end-weights, survival period, heart weights and kidney weights are listed for the animals in which the corresponding pathological finding was diagnosed, they are listed for 4 heart diseases (inflammation of the mitralis, inflammation of the aorta valve, inflammation of the myocardium, necrosis of the myocardium). The average values are calculated separately for the different test groups and the sexes. Only such groups were included in which at least 2 animals demonstrated the stated pathological finding. As a comparison, the weight, respectively the survival period for the total number of animals in the group in question, was listed in each instance.

In the inflammation of the mitralis which occured most frequently in the individual group there appeared no unequivocal difference between the average weight in the partial population of diseased animals and the total average weight. The average values of the partial population fluctuate irregularly around the corresponding total average, whereby deviations upwards are more frequent than deviations downwards. The differences however, are not significant which is attributable in some parts to the low number of animals in the partial test samples.

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Somewhat more unequivocal is the finding for the average survival period which rests above the total average in all groups for the animals with mitralis inflammation. The differences are in parts considerable and are significant particularly in the females (e. g. in the group K: 4, 6, 8, 16). The animals with inflammation of the mitralis have a longer survival period than the rest of the animals.

Source: https://www.industrydocuments.ucsf.edu/docs/ylkk0000

In the heart weight, the average value for the animals with mitralis inflammation rested in almost all the groups above the total average. Only the groups 6 and I3 were an exception. The differences were however mostly not significant. Particularly high differences were found in the groups I, 5, 7, I2, I6, I8 and I8 A.

In the kidney weight, the differences between the partial population with mitralis inflammation and the entire population were less distinct. The values in the population with mitralis inflammation however, rested here too mostly above the total population values. An influence of the treatment could not be established. As far as weight differences were present, they should be predominantly attributable to the more advanced age in the group with mitralis inflammation.

Inflammations of the aorta valve were missing in the groups 2, 4, I3, I6, I7 and I8 A. In the remaining groups, frequently only 3 or 4 animals showed inflammations of the aorta valve. Only among the male animals of group I, there were 6 cases. The comparison of the average values was naturally very uncertain with these low numbers of animals. Therefore, differences could not be ascertained statistically, It is however conspicuous, that the end-weight in the pathological group rests mostly under the total average. The average survival period however, is mostly somewhat higher than in the entire group but the differences are not significant. It is conspicuous, that in group I, the heart weight of the female animals with aorta valve inflammation is considerably higher than the average heart weight of the female animals in this group. However,the kidney weights of these animals rest below the total average. This is an indication of a negative correlation between heart weight and kidney weight, however it could not be statistically ascertained (only two animals showed a pathological finding in this group).

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In the animals with inflammation of the myocardium, it is conspicuous that they have, particularly in the groups K, 2 and 8, a considerably higher end-weight than the total number of animals in these groups. The heart weight and the kidney weight in these groups also climbs above the average weight. However, the number of animals in the pathological

Source: https://www.industrydocuments.ucsf.edu/docs/[illegible]

group is too small to obtain statistically significant results.

In the animals with necroses of the myocardium, the average survival period is significantly higher than the average value in the entire group. The heart weights are also in almost all groups higher for the pathological animals than for the rest. In the kidn r weights, no unequivocal statement can be made on the differences to the total average.

Because of the examinations of the myocardium and the cardiac valves carried out on all animals, it was possible to exclude valve and myocardium diseases as factors for the enlargement of the heart.

In the pathological changes of the muscles of the heart, we made a basic distinction between dystrophic changes of the muscles of the heart which occur in parallelity to skeletal muscle dystrophy and are described in section III, 2 e, and between the myocarditis and severe purulent pericarditis (once among control, once in a treated animal)respectively heart infarcts. Myocardium inflammations were more frequent in the female animals an showed no correlation to the treatment. We observed larger heart infarcts in two animals (ill. 39). These occured in the controls with the same frequency as in the treated animals

In the discussion of the pathology of the heart, blood-forming foci with bone formation and marrow formation occuring in the heart, should be mentioned. In the myocardium of t septum atriorum, there is normally a cartiladge disc in the area of the base of the aorta It will ossify occasionally in older animals whereby blood-forming foci may occur in th area of ossification.

Besides inflammable and degenerative diseases of the cardiovascular system, tumors play a minor part. We found malignant hemangioendotheliomas (ill. 40) and benign hemangiomas (ill. 41)as they were described in similar form in the mouse and the rat, also in the area of the

spleen (see chart 64)

liver (see III/2 b)

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skin - soft tissues (see III/2 k)

uterus (see III/2 h).

Similar tumors had been sporadically observed in the hamster already earlier. FORTNER (I958) saw among 620 hamsters I3 hemangiomas of the spleen, DELLA PORTA (I962) among I9 hamsters I angioma of the spleen, KIRKMAN (I962) among 7200 hamsters 8 hemangiomas of the spleen, LEE and Assoc. (I963) among 54 hamsters 3 hemangiomas of the liver (2) and spleen, SICHUK and Associates (I966) among 79 hamsters I hemangioma of the spleen and TOTH (I967) among 200 hamsters 2 hemangiomas of the liver. In addition, LINDT (I958) described one angioma, VALENTOVA and Assoc. (I962) and KESTERSON and CARLTON (I970) each one hemangioendothelioma.

Upon chronic treatment with DMBA, hemangiomas (liver, spleen, lymph nodes, skin) and hemangioendotheliomas (kidney) were observed by TOTH (I969), RAPPAPORT and Assoc. (I96I) as well as LEE and Assoc. (I963). While malignant vascular tumors occured only sporadically upon treatment with DMBA, RABSON and Assoc. (I960) saw after intratracheal application of polyoma virus among 22 hamsters 9 hemangiomas ~~xxxxxx~~ of the liver besides 6 pavement epithelium carcinomas of the lung.

We found in our experiments no correlation between the formation of the tumors of the cardiovascular system and the treatment. We assume that all discovered tumors are cases of spontaneous tumors.

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Source: https://www.industrydocuments.ucsf.edu/docs/ylkk0000

III.
2 e Dystrophic Myopathy - Cardiomyopathy

Spontaneously appearing degenerative changes in the skeletal muscular system of the goldhamster were apparently first observed by ALTSCHUL (I946). There were already earlier reports (HOUCHIN I942) on the frequent appearance of muscle degeneration in the goldhamster due to vitamin E deficiency. HOMBURGER and Assoc. described I962 a primary degenerative disease of the myocardium and skeletal muscle in an in-bred stock of Syrian goldhamsters. HOMBURGER and BAJUSZ (I970) reported later on a varying occurance of muscular dystrophy in different hamster breeds. The degenerative muscular diseases which often occur simultaneously in the skeletal muscular system and the muscular system of the heart, show considerably varied patterns. Fine granulous calcareous deposits are in parts recognizable in the cloddy, crumbled muscle fibers, in parts, we have simultaneously cloddy decay of the muscular system, so-called Zenker Degeneration, respectively muscle fiber necroses and extensive regenerative processes with connective tissue and cell proliferation as they are also described in human muscular dystrophy and different myopathies of domestic animals (ill. 42 a - c). In the degenerative changes of the myocardium, one often recognizes side by side, all stages of fresh muscular necroses and ossification to connective tissue morbid growth and scar formation. The electronmicroscopic picture of the changes of the muscular system was described by ONISHI and Assoc. (I970)

According to the research of HOMBURGER and BAJUSZ (I970), the changes of the skeletal muscular system as well as those of the myocardium are cases of a genetically conditioned illness which is bound to the X-chromosome. Chart 65 shows the frequency of the degenerative muscle diseases in the skeletal respectively the cardiac muscular system. An influence of the treatment on this hereditary illness could not be proven.

It is conspicuous, that the frequency of cardiomyopathies is considerably larger in the groups I2 - I8 A than in the groups K - II. However, the frequencies for cardiomyopathy as well as for dystrophic myopathy within the groups I - II and within the

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Source: https://www.industrydocuments.ucsf.edu/docs/ylkk0000

groups I2 - I8 do not differ significantly from each other. Since all animals (K - I&A) came from the same breeder and the same colony, only the time of the test begin could be discussed as a reason for the differing frequencies. The groups K - II were delivered in spring (February to March) and the groups I2 - I8 in fall (September). The tests were begun accordingly.

An influence of the smoke-treatment is not provable.

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Source: https://www.industrydocuments.ucsf.edu/docs/yhk0000